



RP, V., V, P., & Hay, A. D. (2016). Are topical antibiotics an alternative to oral antibiotics for children with acute otitis media and ear discharge? *BMJ*, 352, [i308]. <https://doi.org/10.1136/bmj.i308>

Publisher's PDF, also known as Version of record

License (if available):
Unspecified

Link to published version (if available):
[10.1136/bmj.i308](https://doi.org/10.1136/bmj.i308)

[Link to publication record in Explore Bristol Research](#)
PDF-document

© BMJ Publishing Group Ltd 2016. For personal use only.

University of Bristol - Explore Bristol Research

General rights

This document is made available in accordance with publisher policies. Please cite only the published version using the reference above. Full terms of use are available:
<http://www.bristol.ac.uk/red/research-policy/pure/user-guides/ebr-terms/>

PRACTICE



UNCERTAINTIES

Are topical antibiotics an alternative to oral antibiotics for children with acute otitis media and ear discharge?

Roderick P Venekamp *general practitioner and assistant professor*^{1,2}, Vibhore Prasad *general practitioner and clinical assistant professor*³, Alastair D Hay *general practitioner, professor of primary care, and National Institute for Health Research professor*⁴

¹Julius Centre for Health Sciences and Primary Care, University Medical Centre Utrecht, 3508 GA Utrecht, Netherlands; ²Department of Otorhinolaryngology, University Medical Centre Utrecht, Utrecht, Netherlands; ³School of Medicine, University of Nottingham, Nottingham, UK; ⁴Centre for Academic Primary Care, School of Social and Community Medicine, University of Bristol, Bristol, UK

Acute otitis media (AOM) is a common reason for childhood primary care visits and antibiotic prescription in the United Kingdom.^{1,2} Many randomised controlled trials (RCTs) have shown that symptoms settle within a few days, irrespective of antibiotic use,³ with one systematic review reporting that ear pain takes eight days to resolve fully in 90% of children.⁴ However observational data and an individual patient data meta-analysis showed that, among children with AOM, those with ear discharge have a worse prognosis⁵ and a more prolonged duration of ear pain or fever than those without ear discharge.⁶ Current guidance from the UK National Institute for Health and Care Excellence recommends that general practitioners consider immediately prescribing oral antibiotics for children presenting with AOM and ear discharge.⁷

However, oral antibiotics commonly have side effects such as diarrhoea, vomiting, and rashes³ and increase the risk of antimicrobial resistance.⁸ For children with AOM and ear discharge, topical antibiotics are a possible alternative because they put less selective resistance pressure on bacteria and eardrum perforation allows direct entry of the antibiotic into the middle ear, without exposing children to systemic side effects.⁹ However the risk of ototoxicity is debated.^{10,11}

What is the evidence of uncertainty?

To our knowledge, no RCTs or relevant systematic reviews of the effectiveness of topical antibiotics for children with AOM and ear discharge have been published.

Oral antibiotics

By contrast, individual patient data meta-analysis evidence shows that oral antibiotics are more effective than placebo or no treatment in reducing the duration of ear pain and fever in children with AOM and ear discharge; three children need to be treated with oral antibiotics to prevent one child experiencing ear pain or fever at 3-7 days (12/51 (24%) patients taking oral antibiotics v 39/65 (60%) patients taking control treatment).⁶ However, these benefits should be weighed against the possible harms, including systemic side effects and increased risk of antimicrobial resistance.^{3,8} For example, a systematic review reported that 27% of children taking oral antibiotics experienced vomiting, diarrhoea, or rash (283/1044), compared with 20% (208/1063) taking placebo.³

Topical antibiotics

A recent high quality RCT showed that antibiotic-glucocorticoid ear drops (not containing aminoglycosides) are clinically more effective and less costly than oral antibiotics in resolving ear discharge in children with grommets.^{12,13} Because a grommet can be considered a surgically induced eardrum perforation, this indirectly suggests that topical antibiotics may be as effective as oral antibiotics for children with AOM presenting with ear discharge caused by spontaneous perforation of the eardrum.

Various topical antibiotic formulas are available in the UK, including those containing aminoglycosides, quinolones (such as ciprofloxacin with or without dexamethasone), and

Correspondence to: R P Venekamp R.P.Venekamp@umcutrecht.nl

This is one of a series of occasional articles that highlight areas of practice where management lacks convincing supporting evidence. The series advisers are Sera Tort, clinical editor, and David Tovey, editor in chief, the Cochrane Library. To suggest a topic for this series, please email us at uncertainties@bmj.com

What you need to know

- Consider prescribing oral antibiotics immediately for children presenting with acute otitis media and ear discharge caused by spontaneous perforation of the eardrum
- Topical antibiotics are associated with fewer systemic side effects and a lower risk of antibiotic resistance than oral antibiotics, but there is no strong direct evidence to support their use in this condition

chloramphenicol. Of these, quinolone containing drops are considered most appropriate because chloramphenicol has been known to cause sensitivity reactions in children and because of concerns about a link between aminoglycosides and ototoxicity. While animal studies have indicated that aminoglycoside antibiotics are potentially ototoxic when applied directly into the middle ear, the quality of the evidence in humans is debated. The risk of ototoxicity is generally thought to be low when topical antibiotics are used at the time of an active middle ear infection,¹⁰ and there seems to be no such risk for quinolone containing drops.⁹ The *British National Formulary* states that topical aminoglycosides or polymyxins are contraindicated in patients with perforated eardrums or patent ventilation tubes (grommets).¹⁴ By contrast, a UK ear, nose, and throat consensus statement recommends: in “a patient with a discharging ear, in whom there is a perforation or patent grommet: if a topical aminoglycoside is used, this should only be in the presence of obvious infection...[and] for no longer than two weeks.”¹⁰

Is ongoing research likely to provide relevant evidence?

We searched the trial registries “Netherlands Trial Register” (NTR), ClinicalTrials.gov, ISRCTN Register, and metaRegister of Controlled Trials (mRCT) (on 1 June 2015) for completed or ongoing studies on this topic but found no relevant studies.

Our group has submitted grant proposals for two (UK and Netherlands) primary care based, pragmatic, open, two arm, individually randomised, non-inferiority controlled trials to compare the clinical and cost effectiveness of topical and oral antibiotics in children with AOM and ear discharge.

What should we do in the light of the uncertainty?

There is currently no strong direct evidence to support the use of topical antibiotics in children with AOM and ear discharge caused by spontaneous perforation of the eardrum. On the basis of current evidence, and in line with current guidance,⁷ we recommend that doctors consider offering immediate oral antibiotics for these children. That said, doctors who are worried about the adverse effects of oral antibiotics could use the indirect evidence (from children with grommets) to justify the use of topical (non-aminoglycoside) antibiotics.^{12,13} Although anecdotal, our experience suggests that for systemically well children with (otoscopic signs of) ear discharge but no ear pain, a delayed antibiotic strategy with advice about the natural course of the discharge (median duration four days)¹⁵ may be appropriate.

Thanks to all other investigators (Paul Little, Michael Moore, Anne Schilder, Scott Wilkes, Chris Butler, Richard Morris, Nick Francis, Christie Cabral, Jeremy Horwood, Rob Walter, Andrew Lovering, Sandra Hollinghurst, Lindsay Smith, Harriet Downing) and collaborators (Roger

Damoiseaux, Desmond Nunez) of the Painful Runny EAR (PREAR) study team for their valuable input in writing the National Institute for Health Research’s (NIHR) Health Technology Assessment (HTA) programme application. ADH is funded by NIHR Research Professorship (NIHR-RP-02-12-012).

Contributors: ADH and RPV conceived and designed the article. RPV wrote the first draft and VP and ADH commented on it. All authors approved the final version; RPV is guarantor.

Competing interests: We have read and understood BMJ policy on declaration of interests and declare the following interests: RPV has submitted a grant proposal on this topic to the Netherlands Organisation for Health Research and Development (ZonMw) and to the NIHR’s HTA programme. ADH and VP submitted a grant proposal on this topic to the NIHR’s HTA programme. ADH is a member of the NIHR HTA clinical evaluation and trials’ board and chair of the National Institute for Health and Care Excellence antimicrobial stewardship guidelines development group.

Provenance and peer review: Not commissioned; externally peer reviewed.

The views expressed are those of the authors and not necessarily those of the NHS, the NIHR, or UK Department of Health.

Patient consent obtained.

- 1 Royal College of General Practitioners. Research and Surveillance Centre Weekly Returns Service annual report, 2011. <http://bit.ly/1RP0pIW>.
- 2 Gulliford M, Latinovic R, Charlton J, et al. Selective decrease in consultations and antibiotic prescribing for acute respiratory tract infections in UK primary care up to 2006. *J Public Health* 2009;31:512-20.
- 3 Venekamp RP, Sanders S, Glasziou PP, et al. Antibiotics for acute otitis media in children. *Cochrane Database Syst Rev* 2015;6:CD000219.
- 4 Thompson M, Vodicka TA, Blair PS, et al; TARGET Programme Team. Duration of symptoms of respiratory tract infections in children: systematic review. *BMJ* 2013;347:f7027.
- 5 Smith L, Ewings P, Smith C, et al. Ear discharge in children presenting with acute otitis media: observational study from UK general practice. *Br J Gen Pract* 2010;60:101-5.
- 6 Rovers MM, Glasziou P, Appelman CL, et al. Antibiotics for acute otitis media: a meta-analysis with individual patient data. *Lancet* 2006;368:1429-35.
- 7 National Institute for Health and Care Excellence. Respiratory tract infections: prescribing of antibiotics for self-limiting respiratory tract infections in adults and children in primary care. 2008. www.nice.org.uk/guidance/cg69.
- 8 Costelloe C, Metcalfe C, Lovering A, et al. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. *BMJ* 2010;340:c2096.
- 9 Weber PC, Roland PS, Hannley M, et al. The development of antibiotic resistant organisms with the use of otological medications. *Otolaryngol Head Neck Surg* 2004;130:S89-94.
- 10 Phillips JS, Yung MW, Burton MJ, et al. Evidence review and ENT-UK consensus report for the use of aminoglycoside-containing ear drops in the presence of an open middle ear. *Clin Otolaryngol* 2007;32:330-6.
- 11 Llor C, McNulty CA, Butler CC. Ordering and interpreting ear swabs in otitis externa. *BMJ* 2014;349:g5259.
- 12 Van Dongen TM, van der Heijden GJ, Venekamp RP, et al. A trial of treatment for acute otorrhea in children with tympanostomy tubes. *N Engl J Med* 2014;370:723-33.
- 13 Van Dongen TM, Schilder AG, Venekamp RP, et al. Cost-effectiveness of treatment of acute otorrhea in children with tympanostomy tubes. *Pediatrics* 2015;135:e1182-9.
- 14 British National Formulary. British National Formulary; British Medical Association and Royal Pharmaceutical Society of Great Britain. 2014 <http://www.bnf.org/bnf/index.htm>
- 15 Damoiseaux R, van Balen F. Duration of clinical symptoms in children under two years of age with acute otitis media. *Eur Gen Pract* 2000;6:48-51.

Accepted: 17 December 2015

Cite this as: *BMJ* 2016;352:i308

© BMJ Publishing Group Ltd 2016

Methods

We systematically searched PubMed, Embase, NHS-CRD (including DARE, NHS-EED, and HTA), and the Cochrane Library from their inception to 1 June 2015 to identify any published studies comparing the effectiveness of topical antibiotics with oral antibiotics, placebo, or no treatment in children with AOM presenting with ear discharge caused by spontaneous perforation of the eardrum. No relevant published studies were found.

Recommendations for further research

Population: children aged 6 months to 16 years with ear discharge caused by spontaneous perforation of the eardrum and ear pain as the presenting symptoms of acute otitis media (AOM)

Interventions and comparisons: topical antibiotics versus oral antibiotics

Primary outcome: ear pain

Secondary outcomes: duration and severity of systemic (fever, distress or crying, disturbed sleep, interference with normal activity, appetite) and ear (discharge, odour, hearing loss) symptoms; rescue analgesia; adverse events including serious AOM complications (such as mastoiditis, meningitis); recurrences of AOM; NHS resource use; disease specific quality of life using OMQ-14 (for younger children, this can be modified to ear problem related quality of life); antimicrobial resistance; parental satisfaction with treatment allocation and future desire to use ear drops

How patients were involved in the creation of this article

Patient involvement was not sought for this article. However, we sought advice from a patient and public involvement group (including parents of children with ear infections) to formulate our research proposal. This group liked the idea of topical antibiotics as an alternative to oral treatment and thought that ear pain was the most important test of treatment effectiveness because of the distress it causes children and the disruption to family routines (sleep, work, and schooling).

Discussing the uncertainty with patients

Advise parents of children with AOM and ear discharge that guidelines recommend immediately starting oral antibiotics as these have been shown to reduce the duration of ear pain and fever. However, explain that these benefits need to be balanced against possible harms including the risk of side effects, such as diarrhoea, vomiting, and rashes, and increased risk of antimicrobial resistance. Topical antibiotics are associated with fewer side effects and lower risk of antibiotic resistance than oral antibiotics, but there is currently no strong direct evidence to support their use in this condition.